

# PATENT COOPERATION TREATY

## PCT

### NOTIFICATION OF WITHDRAWAL OF PRIORITY CLAIM

(PCT Rule 90bis.3 and  
Administrative Instructions, Section 415(a) and (b))

From the INTERNATIONAL BUREAU

To:

STOTT, Michael, J.  
Glaxo Wellcome plc  
Glaxo Wellcome House  
Berkeley Avenue  
Greenford  
Middlesex UB6 0NN  
ROYAUME-UNI

Date of mailing (day/month/year) 21 January 2000 (21.01.00)	
Applicant's or agent's file reference PU3513	IMPORTANT NOTIFICATION
International application No. PCT/EP99/05271	International filing date (day/month/year) 23 July 1999 (23.07.99)
Applicant GLAXO GROUP LIMITED	

1. The applicant is hereby notified that the priority claim made in the international application has been withdrawn in accordance with a notice of withdrawal received from the applicant on:

20 January 2000 (20.01.00)

The attention of the applicant is drawn to the fact that the withdrawal of the priority claim will result in the re-calculation of time limits which have not already expired (see Rule 90bis.3(d)).

2. ☐ In the case where multiple priorities have been claimed, the above action relates to the following priority claim(s):

3. A copy of this notification has been sent to the receiving Office and to:

- ☒ the International Searching Authority (where the international search report has not yet been issued)
- ☒ the designated Offices (which have already been notified of the receipt of the record copy)
- ☐ the International Preliminary Examining Authority

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Dorothee Mülhausen
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner  
US Department of Commerce  
United States Patent and Trademark  
Office, PCT  
2011 South Clark Place Room  
CP2/5C24  
Arlington, VA 22202  
ETATS-UNIS D'AMERIQUE  
in its capacity as elected Office

Date of mailing (day/month/year) 04 April 2001 (04.04.01)	
International application No. PCT/EP99/05271	Applicant's or agent's file reference PU3513
International filing date (day/month/year) 23 July 1999 (23.07.99)	Priority date (day/month/year)
Applicant KNICK, Vincent, C. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
15 February 2001 (15.02.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Zakaria EL KHODARY Telephone No.: (41-22) 338.83.38
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## PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

To:

STOTT, Michael, J.  
GlaxoSmithKline  
Corporate Intellectual Property  
Two New Horizons Court  
Middlesex TW8 9EP  
ROYAUME-UNI

Date of mailing (day/month/year) 17 August 2001 (17.08.01)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference PU3513	
International application No. PCT/EP99/05271	International filing date (day/month/year) 23 July 1999 (23.07.99)

## 1. The following indications appeared on record concerning:

☐ the applicant      ☐ the inventor      ☒ the agent      ☐ the common representative

Name and Address STOTT, Michael, J. Glaxo Wellcome plc Glaxo Wellcome House Berkeley Avenue Greenford Middlesex UB6 0NN United Kingdom	State of Nationality	State of Residence
	Telephone No. 0171 493 4060	
	Facsimile No. 0181 966 8838	
	Teleprinter No.	

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person      ☐ the name      ☒ the address      ☐ the nationality      ☐ the residence

Name and Address STOTT, Michael, J. GlaxoSmithKline Corporate Intellectual Property Two New Horizons Court Middlesex TW8 9EP United Kingdom	State of Nationality	State of Residence
	Telephone No. 020 8966 8412	
	Facsimile No. 020 8966 8838	
	Teleprinter No.	

## 3. Further observations, if necessary:

## 4. A copy of this notification has been sent to:

<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer  Maria Victoria CORTIELLO
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

STOTT, Michael, J.  
GlaxoSmithKline  
Corporate Intellectual Property  
(CN9.25.1)  
980 Great West Road  
Brentford  
Middlesex TW8 9GS  
ROYAUME-UNI

Date of mailing (day/month/year) 18 February 2002 (18.02.02)	<b>IMPORTANT NOTIFICATION</b>
Applicant's or agent's file reference PU3513	
International application No. PCT/EP99/05271	International filing date (day/month/year) 23 July 1999 (23.07.99)

## 1. The following indications appeared on record concerning:

☐ the applicant ☐ the inventor ☒ the agent ☐ the common representative

Name and Address STOTT, Michael, J. GlaxoSmithKline Corporate Intellectual Property Two New Horizons Court Middlesex TW8 9EP United Kingdom	State of Nationality	State of Residence
	Telephone No. 020 8966 8412	
	Facsimile No. 020 8966 8838	
	Teleprinter No.	

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address STOTT, Michael, J. GlaxoSmithKline Corporate Intellectual Property (CN9.25.1) 980 Great West Road Brentford Middlesex TW8 9GS United Kingdom	State of Nationality	State of Residence
	Telephone No. 020 8047 5000	
	Facsimile No. 020 8047 6894	
	Teleprinter No.	

## 3. Further observations, if necessary:

## 4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned  
☐ the International Searching Authority ☒ the elected Offices concerned  
☒ the International Preliminary Examining Authority ☐ other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Sangeeta JAIYA Telephone No.: (41-22) 338.83.38
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# PCT

## REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference  
(if desired) (12 characters maximum) PU3513

<b>Box No. I</b>	<b>TITLE OF INVENTION</b>		
	Antibody Combination		
<b>Box No. II</b>	<b>APPLICANT</b>		
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below). Glaxo Group Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex, UB6 0NN GB		<input type="checkbox"/> This person is also inventor. Telephone No. 0171 493 4060 Facsimile No. 0181 966 8838 Teleprinter No. 25456	
State (i.e. country) of nationality: GB		State (i.e. country) of residence: GB	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input checked="" type="checkbox"/> all designated States except the United States of America <input type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box			
<b>Box No. III</b>	<b>FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS</b>		
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) KNICK, Vincent C Glaxo Wellcome Inc Five Moore Drive Research Triangle Park NC 27709 US		This person is: <input type="checkbox"/> applicant only <input checked="" type="checkbox"/> applicant and inventor <input type="checkbox"/> inventor only (If this check-box is marked, do not fill in below.)	
State (i.e. country) of nationality: US		State (i.e. country) of residence: US	
This person is applicant for the purposes of: <input type="checkbox"/> all designated States <input type="checkbox"/> all designated States except the United States of America <input checked="" type="checkbox"/> the United States of America only <input type="checkbox"/> the States indicated in the Supplemental Box			
<input checked="" type="checkbox"/> Further applicants and/or (further) inventors are indicated on a continuation sheet.			
<b>Box No. IV</b>	<b>AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE</b>		
The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: <input checked="" type="checkbox"/> agent <input type="checkbox"/> common representative			
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country). STOTT, Michael J Glaxo Wellcome plc Glaxo Wellcome House, Berkeley Avenue Greenford, Middlesex UB6 0NN GB		Telephone No.: 0171-493-4060 Facsimile No.: 0181-966-8838 Teleprinter No.: 25456	
<input type="checkbox"/> Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.			

## Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS

*If none of the following sub-boxes is used, this sheet is not to be included in the request.*

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

STIMMEL, Julie Beth  
Glaxo Wellcome Inc  
Five Moore Drive  
Research Triangle Park  
NC 27709  
US

This person is:

- ☐ applicant only  
☒ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

US

State (i.e. country) of residence:

US

This person is applicant for the purposes of:

☐

all designated States

☐

all designated States except the United States of America

☒

the United States of America only

☐

the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

THURMOND, Linda M  
Glaxo Wellcome Inc  
Five Moore Drive  
Research Triangle Park  
NC 27709  
US

This person is:

- ☐ applicant only  
☒ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

US

State (i.e. country) of residence:

US

This person is applicant for the purposes of:

☐

all designated States

☐

all designated States except the United States of America

☒

the United States of America only

☐

the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only  
☐ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

State (i.e. country) of residence:

This person is applicant for the purposes of:

☐

all designated States

☐

all designated States except the United States of America

☐

the United States of America only

☐

the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

This person is:

- ☐ applicant only  
☐ applicant and inventor  
☐ inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

State (i.e. country) of residence:

This person is applicant for the purposes of:

☐

all designated States

☐

all designated States except the United States of America

☐

the United States of America only

☐

the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. V	DESIGNATION OF STATES
The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):	
<b>Regional Patent</b>	
<input checked="" type="checkbox"/> AP	ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
<input checked="" type="checkbox"/> EA	Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
<input checked="" type="checkbox"/> EP	European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
<input checked="" type="checkbox"/> OA	OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line).....
<b>National Patent (if other kind of protection or treatment desired, specify on dotted line):</b>	
<input checked="" type="checkbox"/> AL	Albania.....
<input checked="" type="checkbox"/> AM	Armenia.....
<input checked="" type="checkbox"/> AT	Austria.....
<input checked="" type="checkbox"/> AU	Australia.....
<input checked="" type="checkbox"/> AZ	Azerbaijan.....
<input checked="" type="checkbox"/> BA	Bosnia and Herzegovina.....
<input checked="" type="checkbox"/> BB	Barbados.....
<input checked="" type="checkbox"/> BG	Bulgaria.....
<input checked="" type="checkbox"/> BR	Brazil.....
<input checked="" type="checkbox"/> BY	Belarus.....
<input checked="" type="checkbox"/> CA	Canada.....
<input checked="" type="checkbox"/> CH and LI	Switzerland and Liechtenstein.....
<input checked="" type="checkbox"/> CN	China.....
<input checked="" type="checkbox"/> CU	Cuba.....
<input checked="" type="checkbox"/> CZ	Czech Republic.....
<input checked="" type="checkbox"/> DE	Germany.....
<input checked="" type="checkbox"/> DK	Denmark.....
<input checked="" type="checkbox"/> EE	Estonia.....
<input checked="" type="checkbox"/> ES	Spain.....
<input checked="" type="checkbox"/> FI	Finland.....
<input checked="" type="checkbox"/> GB	United Kingdom.....
<input checked="" type="checkbox"/> GD	Grenada.....
<input checked="" type="checkbox"/> GE	Georgia.....
<input checked="" type="checkbox"/> GH	Ghana.....
<input checked="" type="checkbox"/> GM	Gambia.....
<input checked="" type="checkbox"/> HR	Croatia.....
<input checked="" type="checkbox"/> HU	Hungary.....
<input checked="" type="checkbox"/> ID	Indonesia.....
<input checked="" type="checkbox"/> IL	Israel.....
<input checked="" type="checkbox"/> IN	India.....
<input checked="" type="checkbox"/> IS	Iceland.....
<input checked="" type="checkbox"/> JP	Japan.....
<input checked="" type="checkbox"/> KE	Kenya.....
<input checked="" type="checkbox"/> KG	Kyrgyzstan.....
<input checked="" type="checkbox"/> KP	Democratic People's Republic of Korea.....
<input checked="" type="checkbox"/> KR	Republic of Korea.....
<input checked="" type="checkbox"/> KZ	Kazakstan.....
<input checked="" type="checkbox"/> LC	Saint Lucia.....
<input checked="" type="checkbox"/> LK	Sri Lanka.....
<input checked="" type="checkbox"/> LR	Liberia.....
<input checked="" type="checkbox"/> LS	Lesotho.....
<input checked="" type="checkbox"/> LT	Lithuania.....
<input checked="" type="checkbox"/> LU	Luxembourg.....
<input checked="" type="checkbox"/> LV	Latvia.....
<input checked="" type="checkbox"/> MD	Republic of Moldova.....
<input checked="" type="checkbox"/> MG	Madagascar.....
<input checked="" type="checkbox"/> MK	The former Yugoslav Republic of Macedonia.....
<input checked="" type="checkbox"/> MN	Mongolia.....
<input checked="" type="checkbox"/> MW	Malawi.....
<input checked="" type="checkbox"/> MX	Mexico.....
<input checked="" type="checkbox"/> NO	Norway.....
<input checked="" type="checkbox"/> NZ	New Zealand.....
<input checked="" type="checkbox"/> PL	Poland.....
<input checked="" type="checkbox"/> PT	Portugal.....
<input checked="" type="checkbox"/> RO	Romania.....
<input checked="" type="checkbox"/> RU	Russian Federation.....
<input checked="" type="checkbox"/> SD	Sudan.....
<input checked="" type="checkbox"/> SE	Sweden.....
<input checked="" type="checkbox"/> SG	Singapore.....
<input checked="" type="checkbox"/> SI	Slovenia.....
<input checked="" type="checkbox"/> SK	Slovakia.....
<input checked="" type="checkbox"/> SL	Sierra Leone.....
<input checked="" type="checkbox"/> TJ	Tajikistan.....
<input checked="" type="checkbox"/> TM	Turkmenistan.....
<input checked="" type="checkbox"/> TR	Turkey.....
<input checked="" type="checkbox"/> TT	Trinidad and Tobago.....
<input checked="" type="checkbox"/> UA	Ukraine.....
<input checked="" type="checkbox"/> UG	Uganda.....
<input checked="" type="checkbox"/> US	United States of America.....
<input checked="" type="checkbox"/> UZ	Uzbekistan.....
<input checked="" type="checkbox"/> VN	Viet Nam.....
<input checked="" type="checkbox"/> YU	Yugoslavia.....
<input checked="" type="checkbox"/> ZW	Zimbabwe.....
Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:	
<input checked="" type="checkbox"/> AE	United Arab Emirates.....
<input checked="" type="checkbox"/> ZA	South Africa.....
<input type="checkbox"/>	.....
<b>Precautionary Designation Statement:</b> In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)	

**Michael J Stott**  
**Agent for the Applicants**

5. International Searching Authority specified by the applicant: **ISA/**

Date of receipt of the record copy  
by the International Bureau

Form PCT/RO/101 (last sheet) (July 1998)



# PCT

## FEE CALCULATION SHEET

Annex to the Request

For receiving Office use only

International application No.

Date stamp of the receiving Office

Applicant's or agent's  
file reference

PU3513

Applicant

Glaxo Group Limited et al

### CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE . . . . .

EUR102

T

2. SEARCH FEE . . . . .

EUR1124

S

Information Search to be carried out by

(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

Basic Fee

The international application 102 sheets.

first 30 sheets . . . . .

EUR413

b<sub>1</sub>

72

x

10

=

EUR720

b<sub>2</sub>

remaining sheets

additional amount

Add amounts entered at b<sub>1</sub> and b<sub>2</sub> and enter total at B . . . . .

EUR1133

B

### Designation Fees

10

x

95

=

EUR950

D

number of designation fees

amount of designation fee

payable (maximum 11)

Add amounts entered at B and D and enter total at I . . . . .

EUR 2083

I

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicant are) so entitled, the total to be entered as I is 25% of the sum of the amounts entered at B and D.

4. FEE FOR PRIORITY DOCUMENT . . . . .

P

5. TOTAL FEES PAYABLE

EUR3309

Add amounts entered at T, S, I and P, and enter total in the TOTAL box

TOTAL

☐ The designation fee is not paid at this time

### MODE OF PAYMENT

☒ authorization to charge  
deposit account (see below)

☐ bank draft

☐ coupons

☐ cheque

☐ cash

☐ other (specify)

☐ postal money order

☐ revenue stamps

Deposit Account Authorization (this mode of payment may not be available at all receiving Offices)

The RO/

☒ is hereby authorized to charge the total fees indicated above to my deposit account.

☒ is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

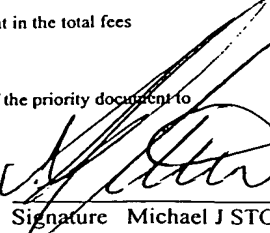
☐ is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

28050185

20 July, 1999

Deposit Account Number

Date (day/month/year)

Signature  Michael J STOTT  
Agent for the Applicants

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

STOTT, Michael J.  
GLAXO WELLCOME PLC  
Glaxo Wellcome House  
Berkeley Avenue  
Greenford  
Middlesex UB6 0NN  
GRANDE BRETAGNE

03 MAY 2001

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing  
(day/month/year)

03.05.2001

Applicant's or agent's file reference  
PU3513

## IMPORTANT NOTIFICATION

International application No.  
PCT/EP99/05271

International filing date (day/month/year)  
23/07/1999

Priority date (day/month/year)  
27/07/1998

Applicant  
GLAXO GROUP LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

## 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
Fax: +49 89 2399 - 4465

Authorized officer

Neumann, M

Tel. +49 89 2399-7351



# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>PU3513</b>	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/EP99/05271</b>	International filing date (day/month/year) <b>23/07/1999</b>	Priority date (day/month/year) <b>27/07/1998</b>
International Patent Classification (IPC) or national classification and IPC <b>A61K39/395</b>		
Applicant <b>GLAXO GROUP LIMITED et al.</b>		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 9 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand <b>15/02/2001</b>	Date of completion of this report <b>03.05.2001</b>
Name and mailing address of the international preliminary examining authority:  <b>European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465</b>	Authorized officer <b>Mennessier, T</b>  Telephone No. +49 89 2399 8687



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP99/05271

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-34 as originally filed

**Claims, No.:**

1-15 as originally filed

**Drawings, sheets:**

1/24-24/24 as originally filed

**Sequence listing part of the description, pages:**

1-37, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP99/05271

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:  
**see separate sheet**

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.  
☒ claims Nos. 12-14.

because:

- ☒ the said international application, or the said claims Nos. 12-14 (with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.  
☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/05271

## 1. Statement

Novelty (N)	Yes:	Claims	4-6 and 13
	No:	Claims	1-3, 7-12, 14 and 15
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-15
Industrial applicability (IA)	Yes:	Claims	1-11 and 15
	No:	Claims	

## 2. Citations and explanations

**see separate sheet**

## VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:  
**see separate sheet**

## VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP99/05271

1. Documents cited in this written opinion

Reference is made to the following documents:

- # D1: *Hybridoma*, 5(suppl. 1), 1986, S171-4,  
XP000881980
- # D2: *International Journal of Cancer*, 71(2), 1997, 237-45,  
XP000882050
- # D3: *Cancer Investigation*, 17(suppl. 1), 1999, 32-34,  
XP000882015

2. Comments with respect to item III

**Claims 12-14** relate to methods of treatment of the body by therapy, i.e., to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

3. Comments with respect to item V

a) Novelty (Article 33(2) PCT)

Document D1 (see the whole document) discloses a "combination" consisting of an 17-1A monoclonal antibody and three chemotherapeutic agents, namely 5-fluorouracil, Adriamycin and mitomycin, as generally defined in **claims 1 and 2**. Therefore, the subject-matter of the said claims lacks novelty. As the term "Panorex" referred to in claim 3 is used to designate a particular 17-1A antibody, also the subject-matter of claim 3 is not new. As the cells treated in document D1 are adenocarcinoma cells capable of metastasing, the same conclusion also applies to claims 7-9. As the "combination" of drugs was used in D1 to treat advanced pancreatic carcinoma, the subject-matter of claims 10-12, 14 and 15 is considered to lack novelty.

b) Inventive step (Article 33(3) PCT)

- (i) The present comments are made with respect to claims for which novelty can be acknowledged, i.e., claims 4, 5, 6 and 13.
- (ii) It may be considered that a skilled person aware of document D1 would be prompted to test further chemotherapeutic agents available to him at the priority date in view of preparing a further "combination" as already described in D1 and to test it as also done in D1 in the treatment of tumoral cells. Therefore, the subject-matter of claims 4 and 5 appears not to involve an inventive step.
- (iii) Novelty of claim 13 has been acknowledged on the basis of an additional technical feature which is based on the measuring of a parameter which had not been taken into consideration by the authors of document D1. In the absence of any data suggesting that binding of the 17-1A monoclonal antibody of document D1 would not be less than between 2 to 10 fold compared to binding in the absence of a chemotherapeutic agent to be used in combination, it cannot be concluded that the subject-matter of claim 13 involves an inventive step.
- (iv) Moreover, the point has to be stressed that in document D2 (see the two chapters entitled "Modulation of antigen expression" on pages 238-239 and pages 239-240, respectively) it has been unambiguously established that pre-incubation of two tumour cell lines in presence of 5-fluorouracil results in an increase in EGP40 expression, which is a clear indication to a person skilled in the art, that administration of a "combination" as defined in claim 1, of which the chemotherapeutic agent being administered prior to the antibody (see point 6(b) below), [the only administration mode of the invention for which a true support exists in the description] would reasonably be more efficient than administration of the antibody alone. The said person would therefore not have regarded as surprising the finding (as referred to in the paragraph bridging pages 3 and 4 of the description) on which the



invention as a whole has been said to rely.

- (iv) In view of the above remarks, it is therefore considered that none of the claims involves an inventive step.

c) Industrial applicability (Article 33(4) PCT)

- (i) The subject-matter of **claims 1-11 and 15** is considered to be susceptible of industrial applicability.
- (ii) For the assessment of the present **claims 12-14** and also **claims 10-11** on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

d) P-document

Should the priority appear not to have been validly claimed, document D3 would have to be taken into consideration when examining whether the various aspects of the claimed invention are new and involve an inventive step.

4. Comments with respect to item VII

- a) In **claims 4 and 5** the use of abbreviations (see the terms "UFT, CPT-II, 5FU") to designate chemotherapeutic agents should be avoided. The same also applies to trademarks (see the term "Raloxiden").
- b) The use of the terms "*continuous infusion*" in each of **claims 4 and 5**, and of the term "*iv and oral*" in claim 4 appears to be irrelevant.

- c) Taken into consideration the fact that in **claim 4** which is dependent on **claim 1** the chemotherapeutic agent referred to is defined as consisting of one or more agents, in order to avoid any ambiguity it would have been more appropriate to indicate in **claim 1** that the subject-matter for which protection is sought is a combination of an antibody "with one or more chemotherapeutic agents".

5. Comments with respect to item VIII

- a) Due to the use of the term "*combination*", which appears in the present context to be vague and indefinite, **claims 1-9** are objected to under Article 6 PCT. Reformulation of the said claims in such a way that they appear to be unambiguously directed to a preparation in the form of a "kit-of-parts", of which the components formed a functional unity through a purpose-directed application, would overcome the objection.
- b) What the description clearly establishes (see Examples 2 to 5) is that pre-treatment of tumour cells with a chemotherapeutic agent known to block cell cycle progression at S and/or G<sub>2</sub>/M results in a significant increase in the density of the Ep-CAM antigen population and thus in greater targeting of anti-Ep-CAM antibodies to Ep-CAM expressing tumours. This is the gist of the invention, see further the paragraph bridging pages 3 and 4 of the description. It has not been established elsewhere in the description how a chemotherapeutic agent and an anti-Ep-CAM antibody could react synergistically in the case where either the agent and the antibody are administered simultaneously or the antibody is administered prior to the agent. Therefore, administration of the agent prior to the antibody has to be regarded as an technical feature that is essential to the performance of the invention and as such should be present in each of use and method **claims 10-14**, which presently are objected to under Article 6 PCT as not containing the said feature.
- c) **Claim 15** appears to lack clarity due to the omission of a verb after the term "*composition*". Moreover, in order to meet the requirements of Article 6 PCT, for the reasons explained above, **claim 15** should be re-formulated in such a

way that it is clearly specified that the claimed composition contains both an antibody and a chemotherapeutic agent which are physically separated, the said separation allowing the agent to be administered prior to the antibody.

- d) The wording of **claim 5** appears to be confusing due to the use of the term "*and*". It is not clear whether the claimed combination comprises only one of the listed chemotherapeutic agents or each of them. For that reason, **claim 5** is also objected to under Article 6 PCT.
- e) According to page 7, lines 28-30 "*throughout the specification the term chemotherapeutic can [therefore] be substituted with "radiotherapy"*". This appears to be a non-admissible statement, as, indeed, chemotherapy and radiotherapy involve two distinct treatments, each of the terms having a well- recognized specific meanings. If the Applicants were intended to seek protection for the use of an antibody as defined in claim 1 in combination with radiotherapy, they should have filed further claims specifically directed to that subject-matter. Nevertheless, in the absence of any experimental evidence elsewhere in the description with regard to the said subject-matter, said claims would have been considered not to be supported by the description. In order to avoid any discrepancy between the claims and the description, the whole paragraph of the description on page 7, lines 25-30 should be deleted.

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>PU3513</b>	<b>FOR FURTHER ACTION</b> <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. <b>PCT/EP 99/05271</b>	International filing date (day/month/year) <b>23/07/1999</b>	(Earliest) Priority Date (day/month/year) <b>27/07/1998</b>
Applicant  <b>GLAXO GROUP LIMITED et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

### 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**COMBINATION OF AN ANTI-EP-CAM ANTIBODY WITH A CHEMOTHERAPEUTIC AGENT**

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ **None of the figures**

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 99/05271

## Box I Observations where certain claims were found uns searchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 12-14 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the co-administered chemotherapeutic agent and anti-Ep-CAM antibody.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International Application No

EP 99/05271

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K39/395 //A61K38:16,A61K31:00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>PAUL A R ET AL: "Treatment of advanced measurable or evaluable pancreatic carcinoma with 17-1A murine monoclonal antibody alone or in combination with 5-fluorouracil, adriamycin and mitomycin (FAM)."</p> <p>HYBRIDOMA, (1986 JUL) 5 SUPPL 1 S171-4. , XP000881980</p> <p>the whole document</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	1-15

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*G\* document member of the same patent family

Date of the actual completion of the international search

20 March 2000

Date of mailing of the international search report

14. 04. 00

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax: (+31-70) 340-3016

Authorized officer

Mennessier, T

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 99/05271

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KIEVIT E ET AL: "Determination of tumor-related factors of influence on the uptake of the monoclonal antibody 323/A3 in experimental human ovarian cancer." INTERNATIONAL JOURNAL OF CANCER, (1997 APR 10) 71 (2) 237-45. , XP000882050 page 238, right-hand column -page 240, left-hand column page 243; table III ---	1-15
Y	BOKEMEYER C ET AL: "[Current aspects of adjuvant and palliative chemotherapy in colorectal carcinoma]. Aktuelle Aspekte zur adjuvanten und palliativen Chemotherapie beim kolorektalen Karzinom." SCHWEIZERISCHE RUNDSCHAU FUR MEDIZIN PRAXIS, (1997 SEP 24) 86 (39) 1510-6 REF: 11 , XP000882022 page 1515, paragraph 3.4; table 8 ---	1-15
Y	CASILLAS S ET AL: "Adjuvant therapy for colorectal cancer: present and future perspectives." DISEASES OF THE COLON AND RECTUM, (1997 AUG) 40 (8) 977-92. REF: 80 , XP000882030 page 989, left-hand column page 980; table 1 ---	1-15
Y	EP 0 252 741 A (CENTOCOR INC) 13 January 1988 (1988-01-13) page 2, line 58-63 page 3, line 8-13 ---	1-15
A	BLEIBERG H: "Continuing the fight against advanced colorectal cancer: new and future treatment options." ANTI-CANCER DRUGS, (1998 JAN) 9 (1) 18-28. REF: 83 , XP000882025 page 23 page 24; table 1 ---	1-15
A	ELIAS D J ET AL: "Monoclonal antibody KS1/4-methotrexate immunoconjugate studies in non-small cell lung carcinoma." AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE, (1994 OCT) 15 (4) 1114-22. , XP000882026 page 1114 page 1121, left-hand column ---	1-15
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## INTERNATIONAL SEARCH REPORT

International Application No

P/SEP 99/05271

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HAISMA H J ET AL: "A monoclonal antibody-beta-glucuronidase conjugate as activator of the prodrug epirubicin-glucuronide for specific treatment of cancer." BRITISH JOURNAL OF CANCER, (1992 SEP) 66 (3) 474-8. , XP000882039 the whole document ---	1-15
P,X	SCHWARTZBERG, LEE S. (1): "Chemotherapy plus PANOREX (17-1A monoclonal antibody) as adjuvant therapy for colon cancer: Ongoing studies." CANCER INVESTIGATION, (1999) VOL. 17, NO. SUPPL. 1, PP. 32-34. MEETING INFO.: XVI CHEMOTHERAPY FOUNDATION SYMPOSIUM ON INNOVATIVE CANCER THERAPY FOR TOMORROW NEW YORK CITY, NEW YORK, USA NOVEMBER 11-13, 1998 CHEMOTHERAPY FOUNDATION. , XP000882015 the whole document -----	1-15



# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

EP 99/05271

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0252741 A	13-01-1988	AT 159174 T	15-11-1997
		DE 3752129 D	20-11-1997
		DE 3752129 T	07-05-1998
		EP 0755683 A	29-01-1997
		ES 2110392 T	16-02-1998
		GR 3025902 T	30-04-1998
		HK 1002829 A	18-09-1998
		JP 2979318 B	15-11-1999
		JP 63060941 A	17-03-1988
		JP 2000026312 A	25-01-2000
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# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

# PCT

To:  
GLAXO WELLCOME PLC  
Glaxo Wellcome House  
Attn. STOTT, Michael J.  
Berkeley Avenue  
Greenford  
Middlesex UB6 0NN  
UNITED KINGDOM

<b>Global Intellectual Property</b>		
RECEIVED	17 APR 2000	INIT
ACTION	ATTN	FILE
14/6/00	GN	GW

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT  
OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing  
(day/month/year) 14/04/2000

Applicant's or agent's file reference

PU3513

**FOR FURTHER ACTION**

See paragraphs 1 and 4 below

International application No.

PCT/EP 99/05271

International filing date  
(day/month/year)

23/07/1999

Applicant

GLAXO GROUP LIMITED et al.

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Véronique Baillou

## NOTE FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

##### Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

**"Statement under article 19(1)" (Rule 46.4)**

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

**It must be in the language in which the international application is to be published.**

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

**Consequence if a demand for international preliminary examination has already been filed**

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

**Consequence with regard to translation of the international application for entry into the national phase**

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.